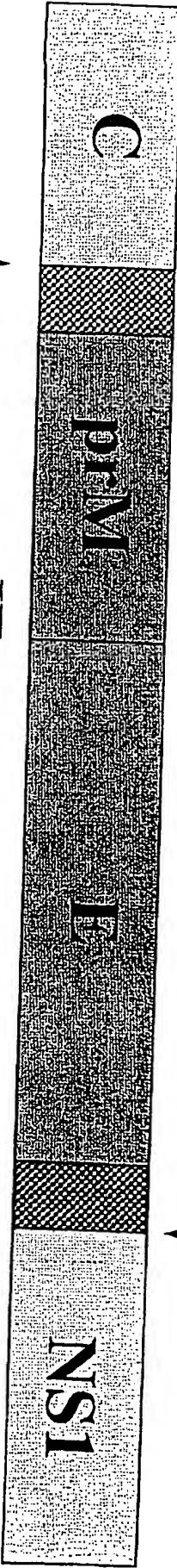


Junction sequences of ChimeriVax™-JE (YF/JE) virus

Signalase

YAGA	MKL	JE	TNVHA	DTGCA
MTGG	VTL	YF	LGVGA	DQGCA
MTGG	MKL	YF/JE	TNVGA	DQGCA



NS2B-3 protease*

NKR → CGNE JE
 KRR → SHDV YF
 KRR → SHDV YF/JE

*: This cleavage is prerequisite for efficient signalase-mediated processing at the C/prM junction

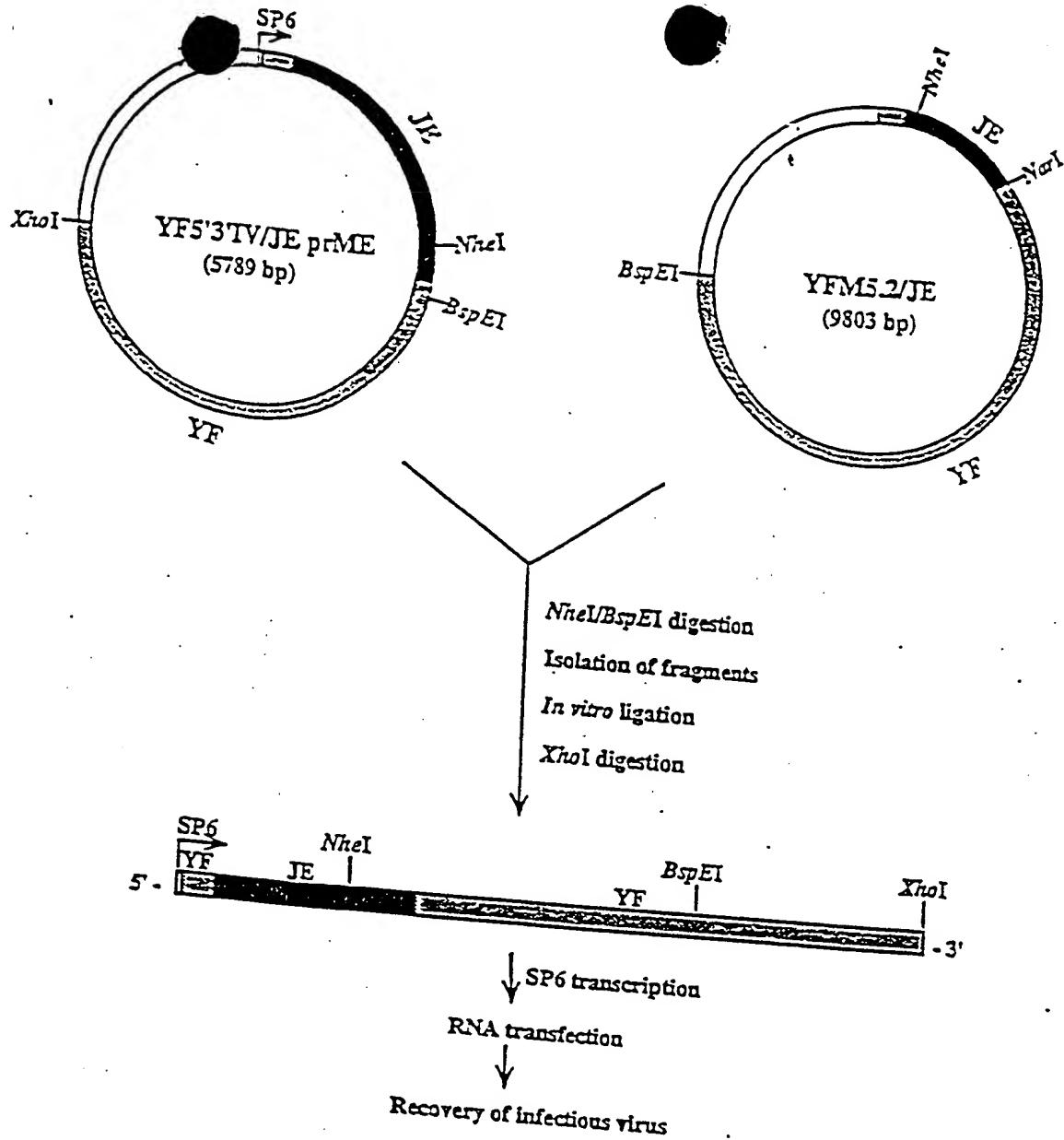


Fig. 2

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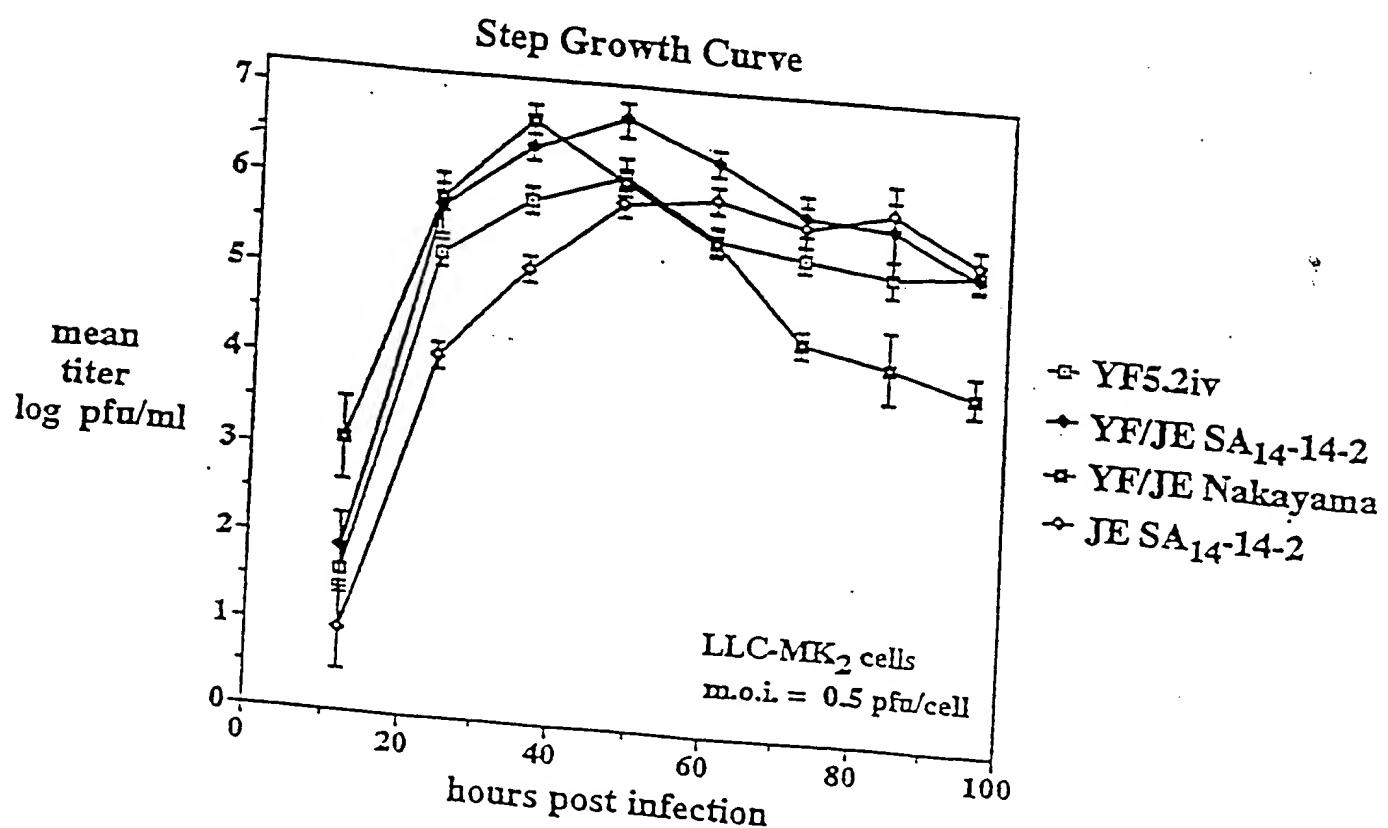
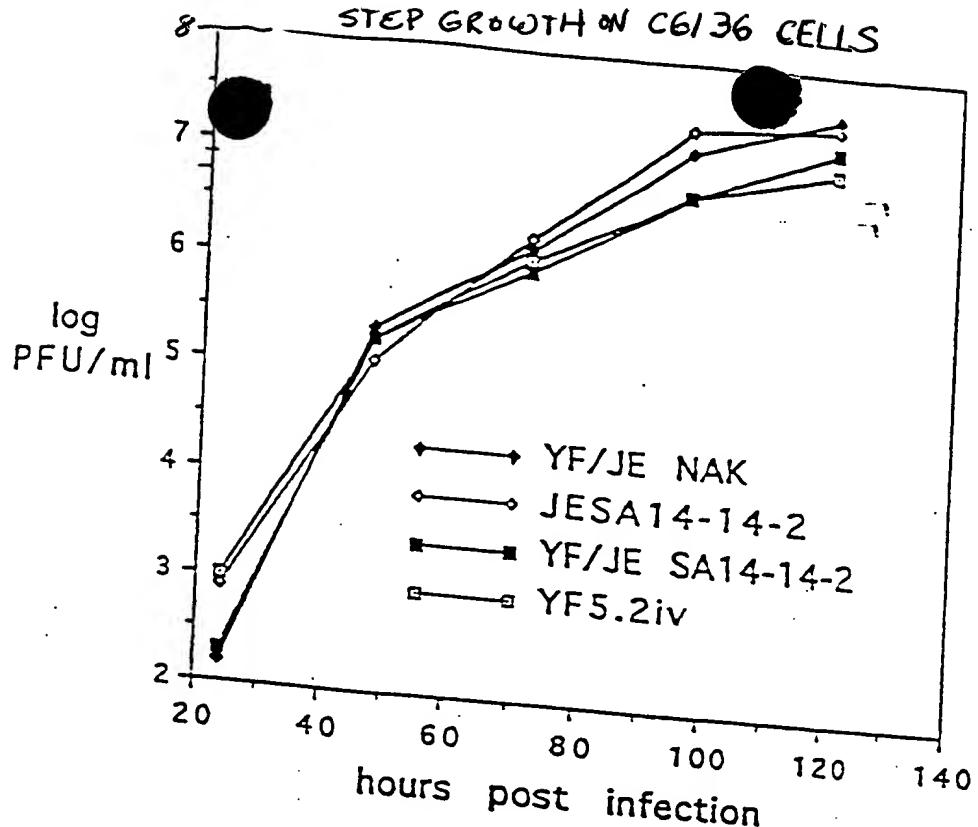


Fig 3

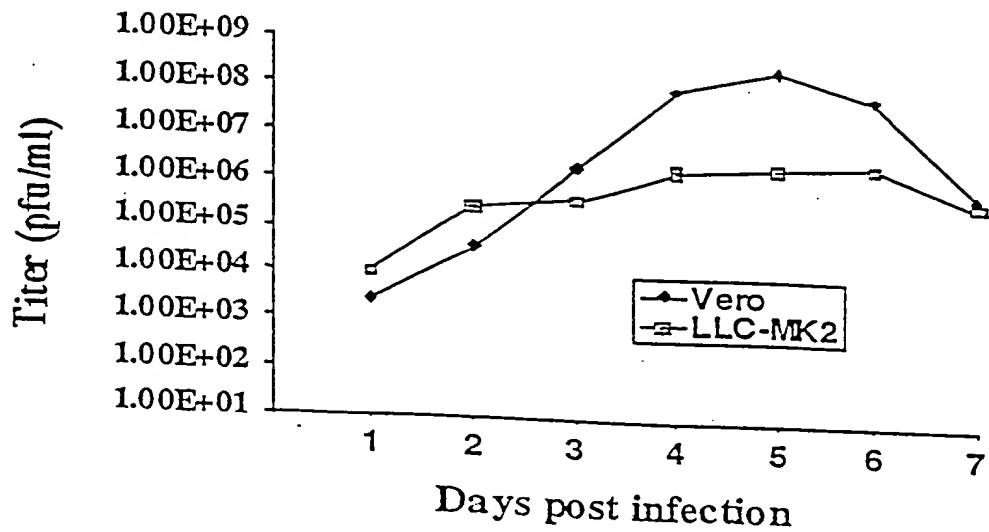
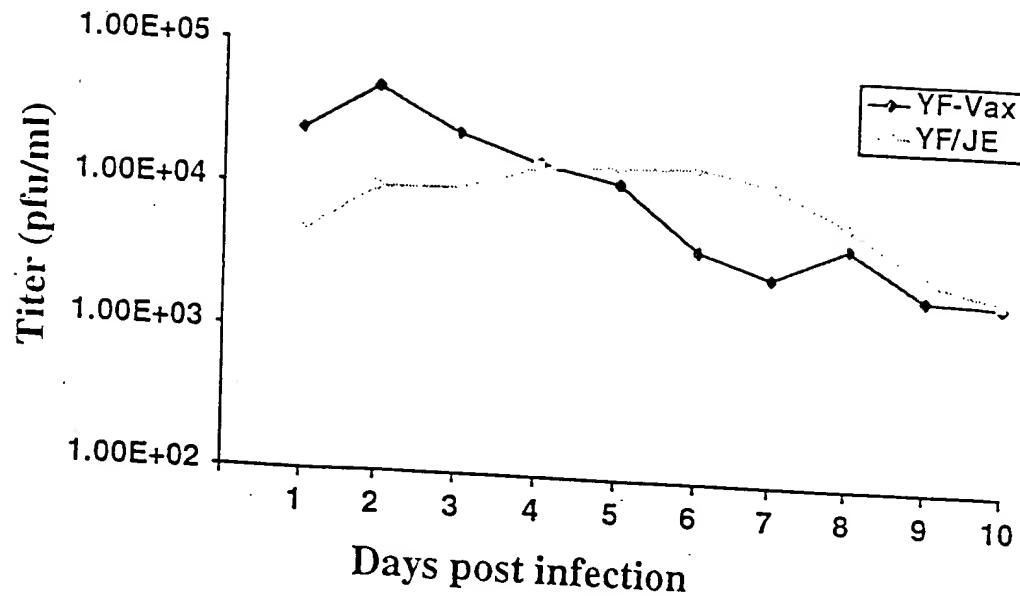


Fig. 4. Growth curves of RMS (YF/JE_{SA14142}) in Vero and LLC-MK2 cells.



Growth comparison between RMS and YF-Vax in MRC-5 cells.

Fig.5

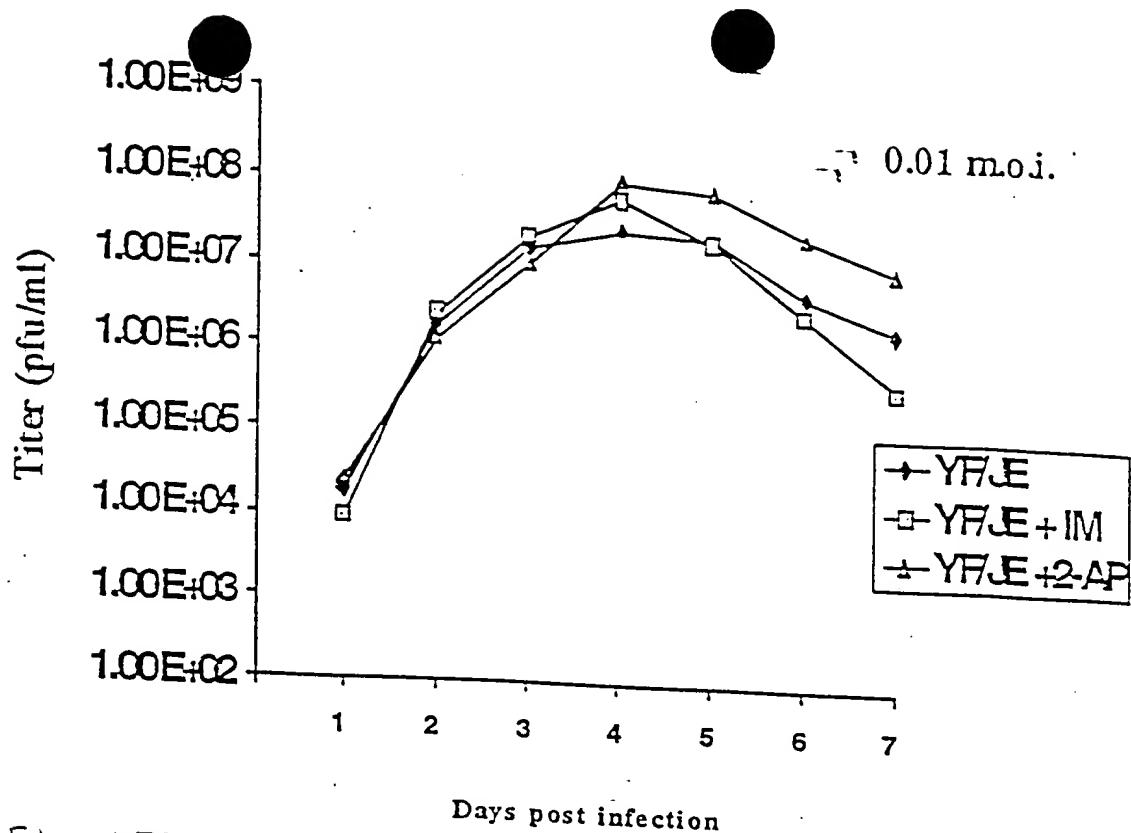


Fig. 6A. Effect of indomethacin (IM) or 2-aminopurine (2-AP) on growth kinetics of YF/JE SA14-14-2 (0.01 MOI) in FRhL cells

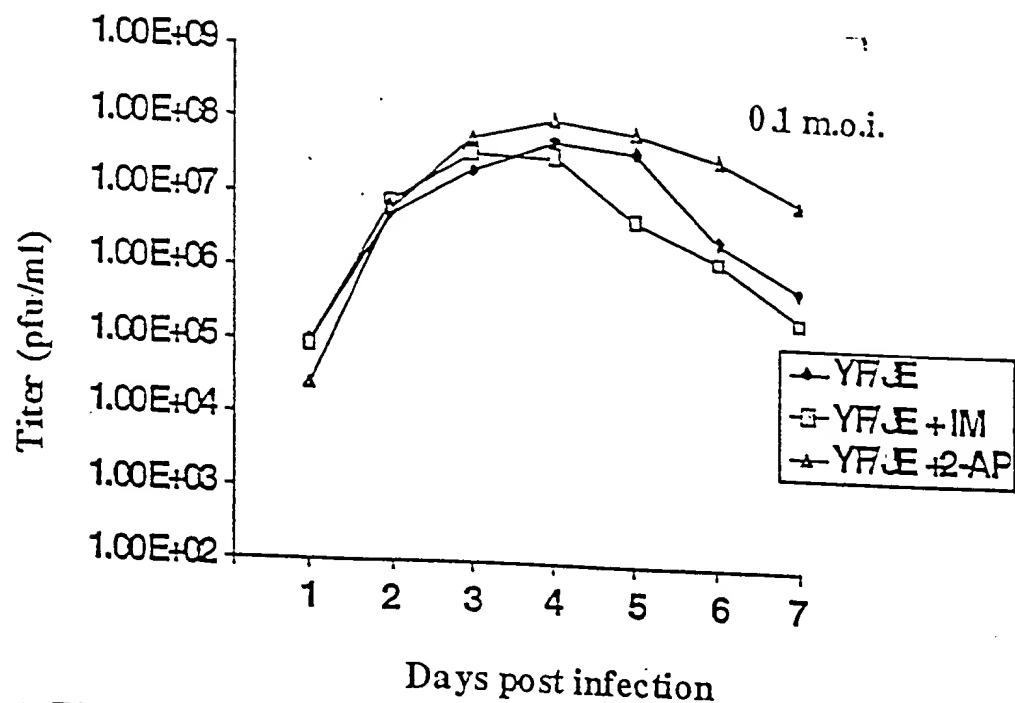
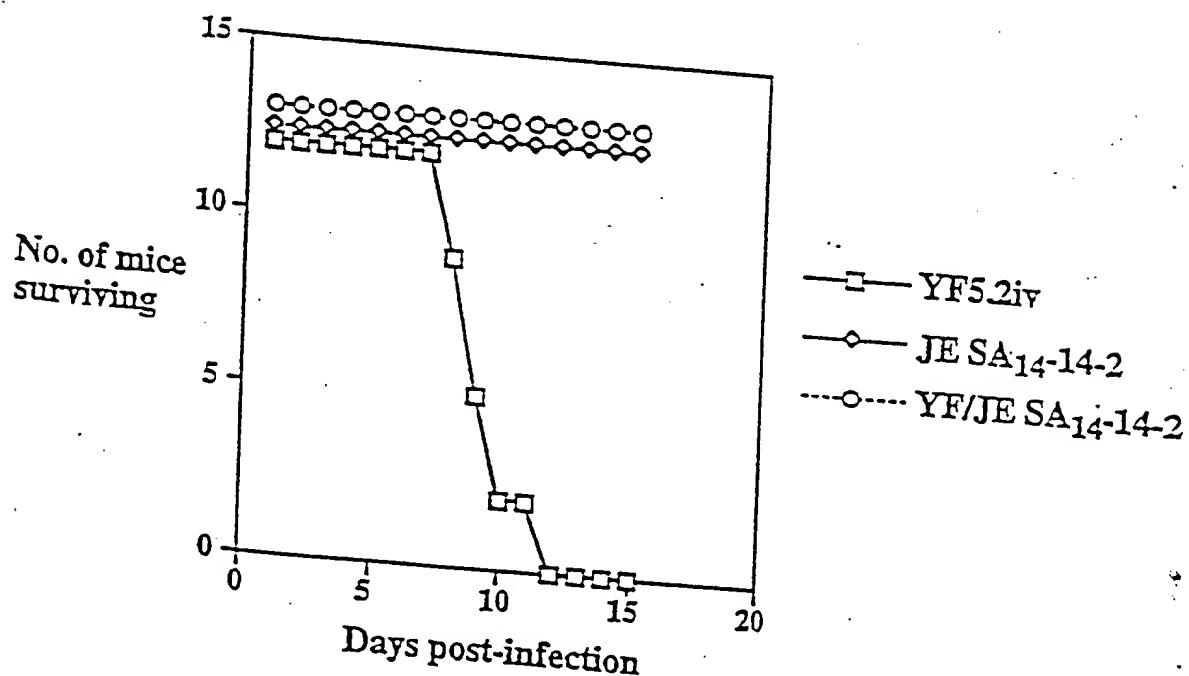


Fig. 6.2 Effect of indomethacin or 2-aminopurine on growth kinetics of YF/JE_{SA14142} (0.1 MOI in FRhL cells.

Mouse neurovirulence analysis

MICE:

VIRUS DOSE: 4 week old ICR males/females
 10^4 pfu intracerebrally



Virus	Survival	P
YF5.2iv	0/12 (0%)	-
JE SA ₁₄₋₁₄₋₂	12/12 (100%)	<0.001
YF/JE SA ₁₄₋₁₄₋₂	13/13 (100%)	<0.001

Fig. 7

216 E 212 Q " X 85 T 2 T 6 0

Neutralizing antibody response
to YF/JE SA14-14-2 chimeric vaccine
(3-week old mice immunized, samples for testing taken at 6 weeks)

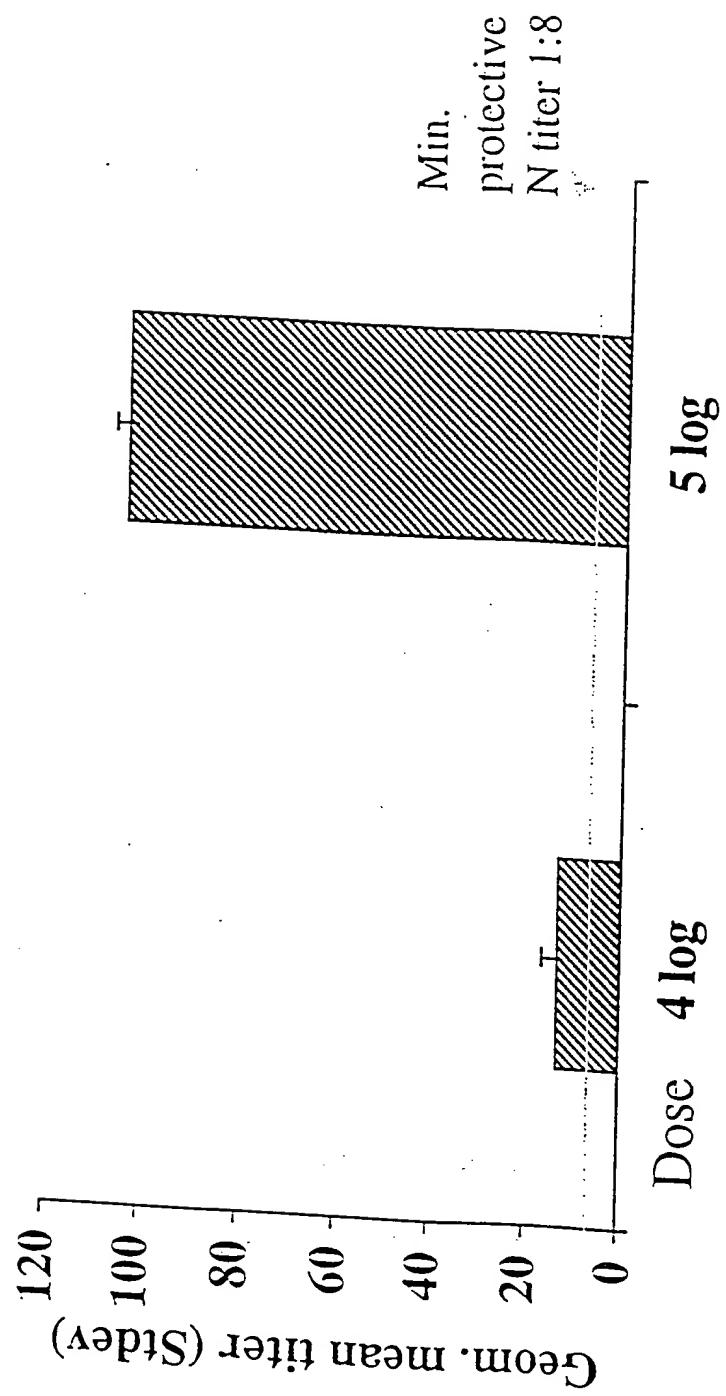


Fig. 8

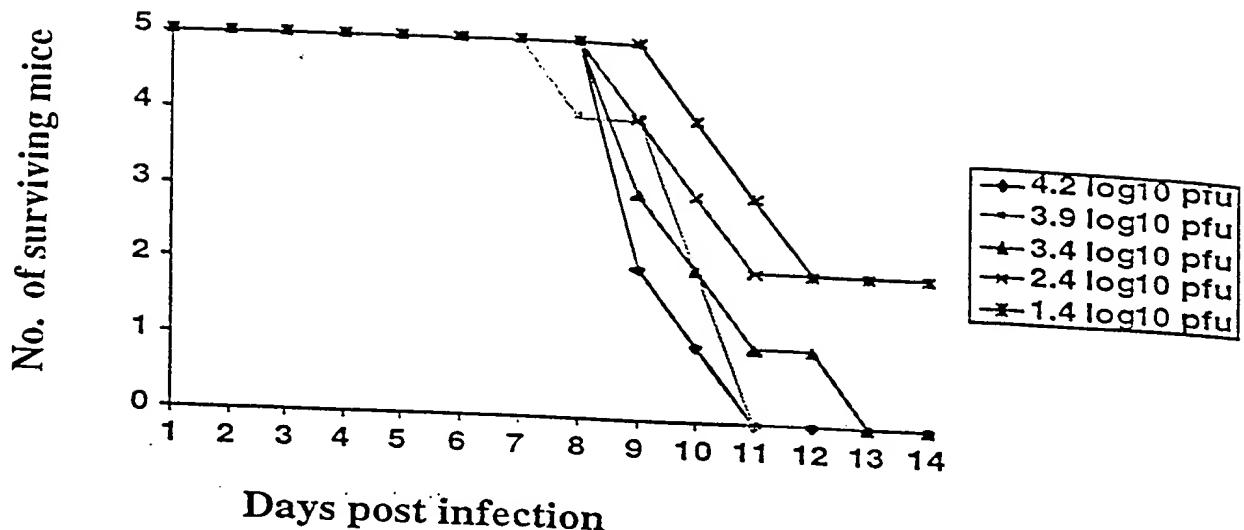


Fig. 9A. Neurovirulence testing of YF-Vax in 4-week old ICR mice by the i.c. route

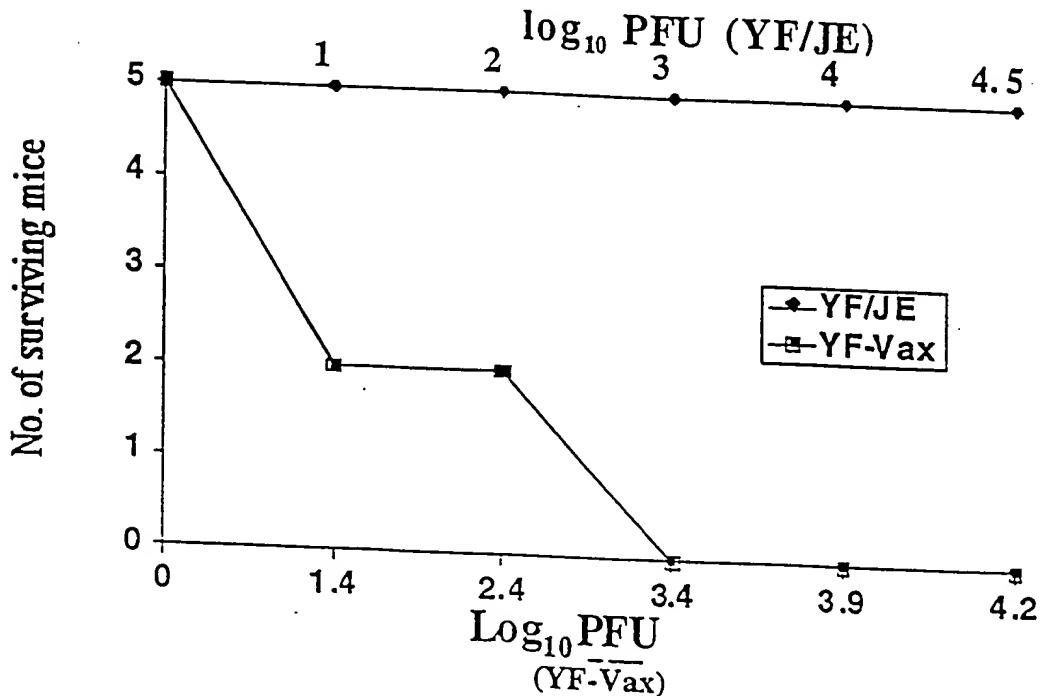


Fig. 9B. Neurovirulence testing of YF/JE_{SA14-14-2} in 4-week old ICR mice by I.C. route

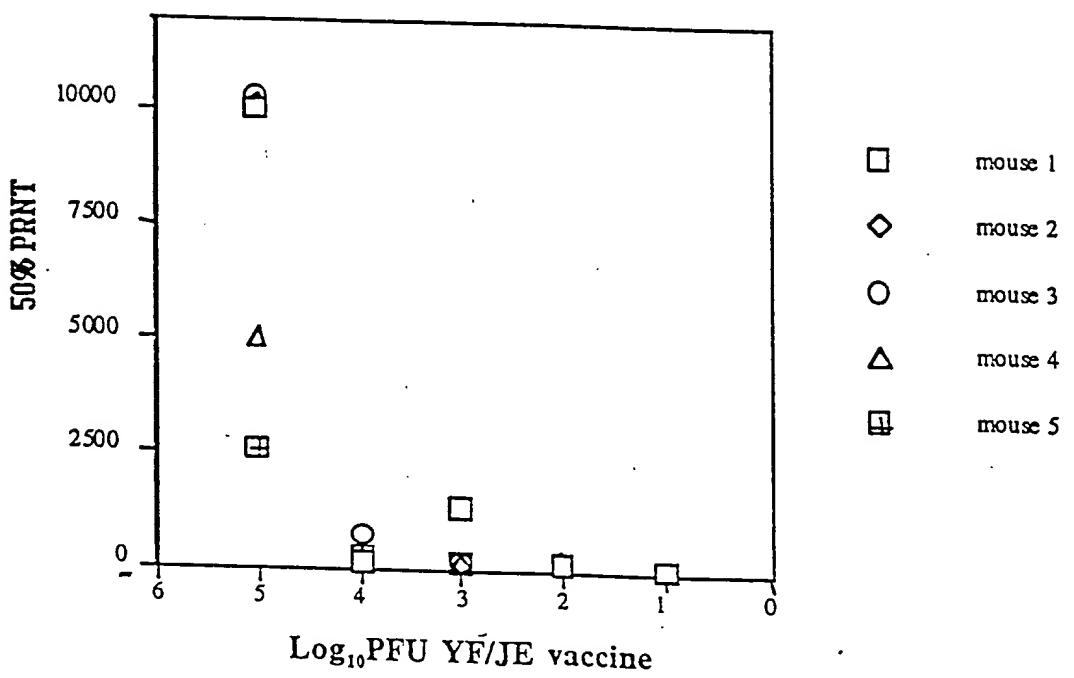
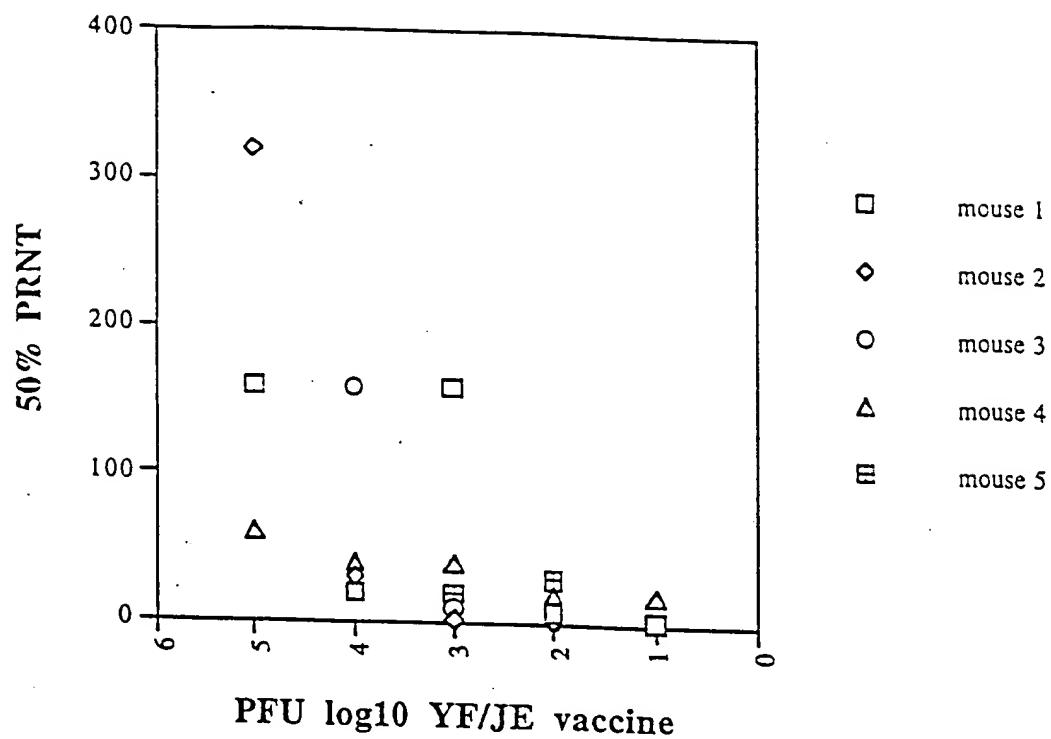
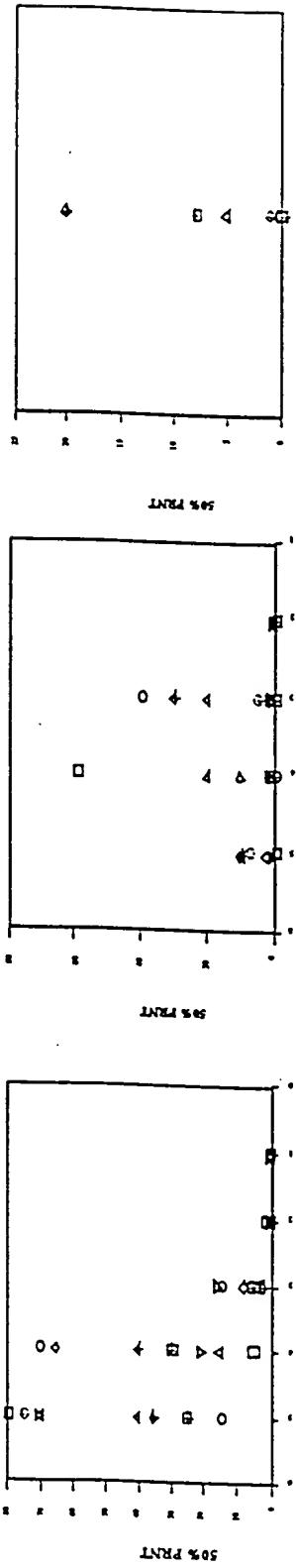


Fig. 10 Neutralizing antibody titers in mice inoculated s.c. with graded doses of YF/JE vaccine. TOP: 3 weeks post immunization and BOTTOM: 8 weeks post immunization

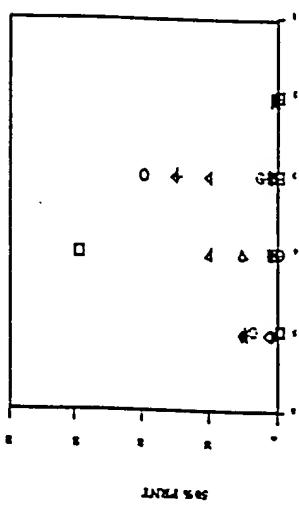
215 222 227 230 235 240 245 250

ChimeriVax™

JE-Vax®

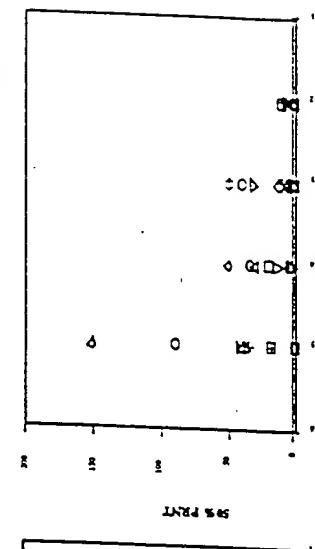
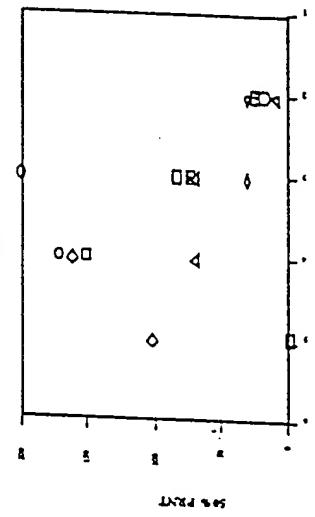


SA14-14-2 (BHK1)



YF/Nakayama

YF5.2 (17D Inf. clone)



JE Nakayama

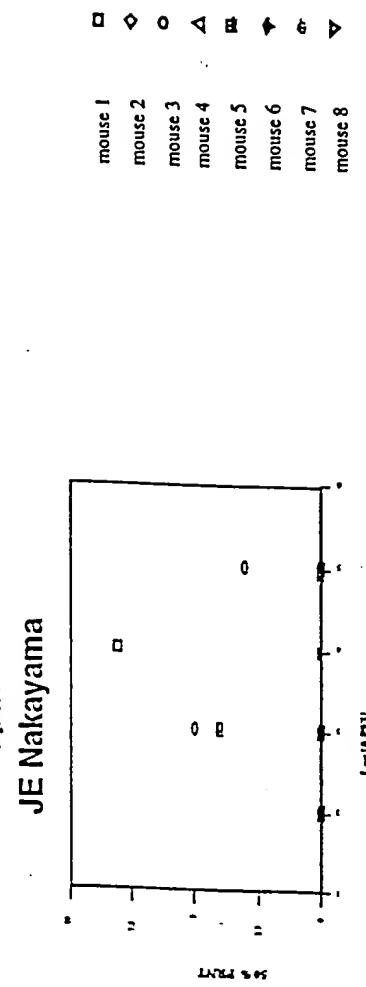


Fig. 1. SEROLOGICAL RESPONSES OF MICE IMMUNIZED WITH A SINGLE DOSE OF LIVE VIRUSES

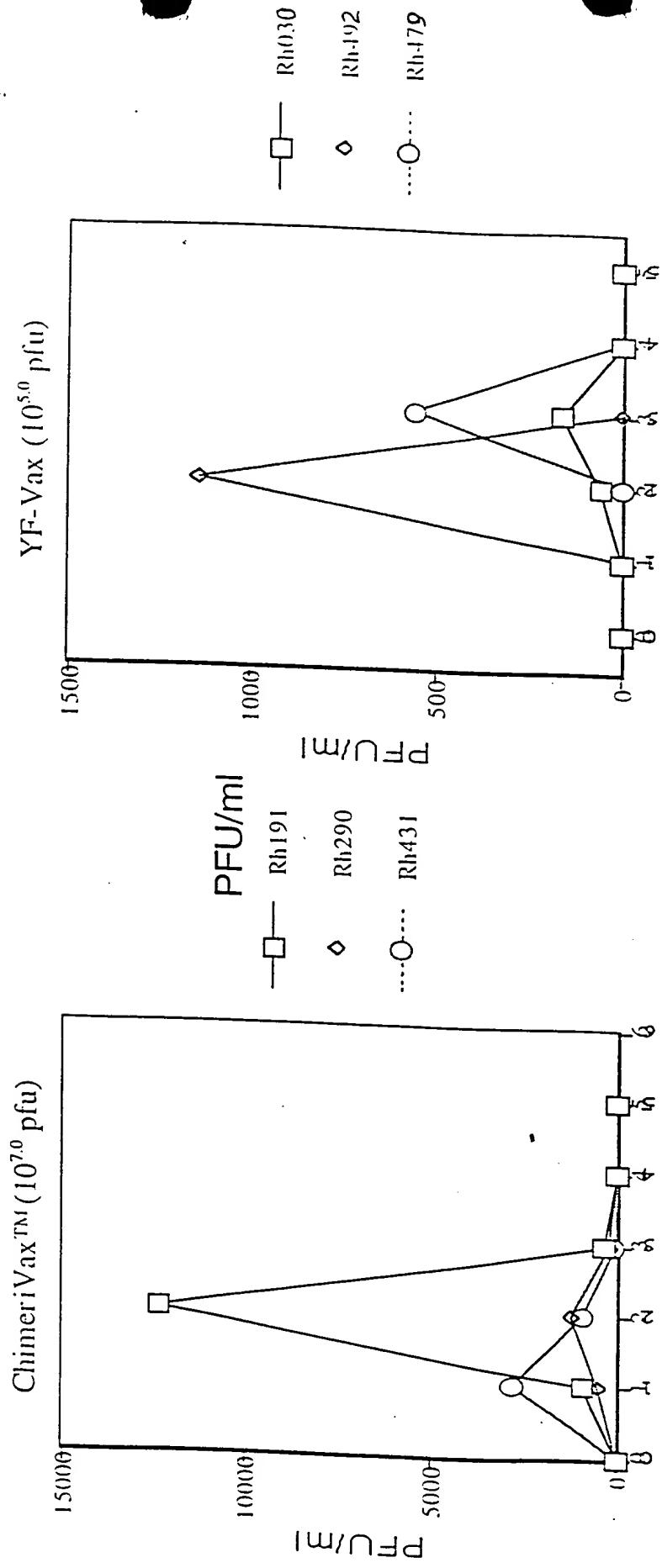


Fig. 12. Viremia and GMT of viremia in 3 rhesus monkeys inoculated with ChimериVax™ or YF-Vax® by the I.C. route.

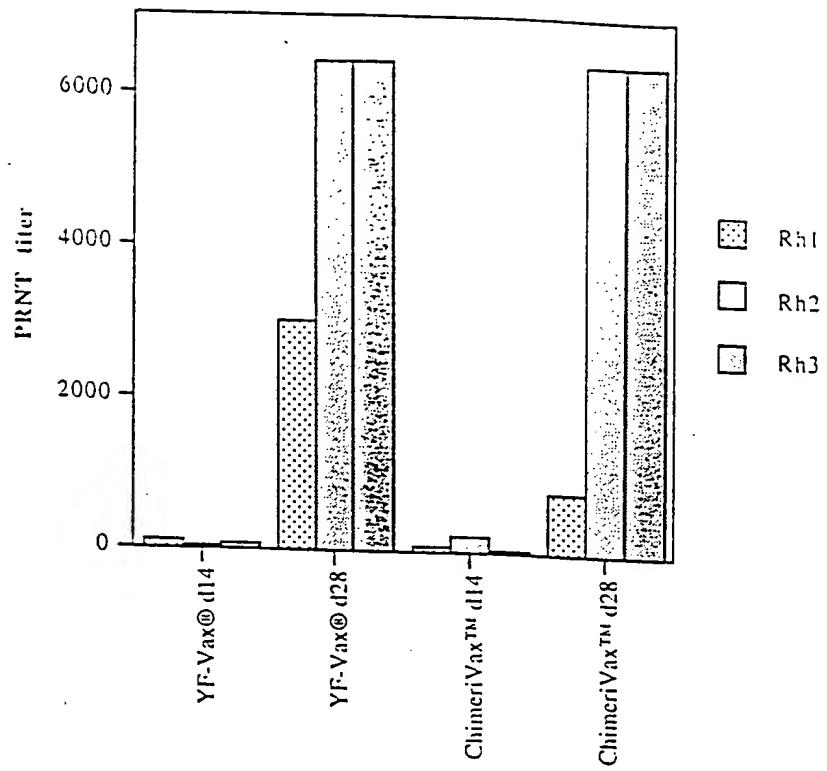


Fig. 13 Neutralizing antibody titers (50%) in rhesus monkeys 2 and 4 weeks post inoculations with a single dose of vaccines by the I.C. route.

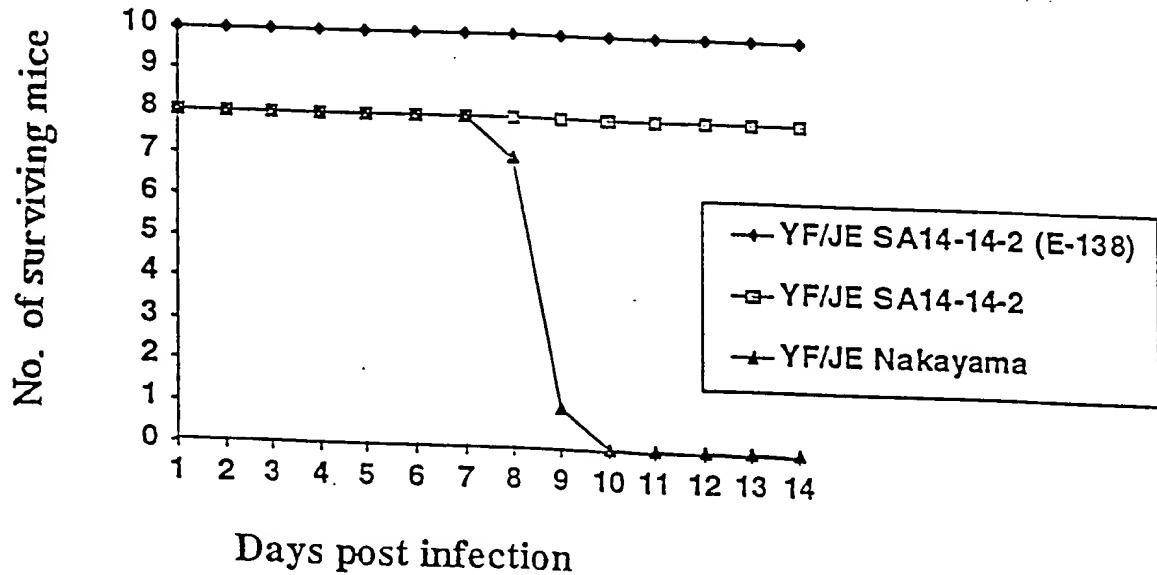


Fig. 14 Mouse neurovirulence testing of YF/JE SA14-14-2 (E-138 K-->E) mutant.

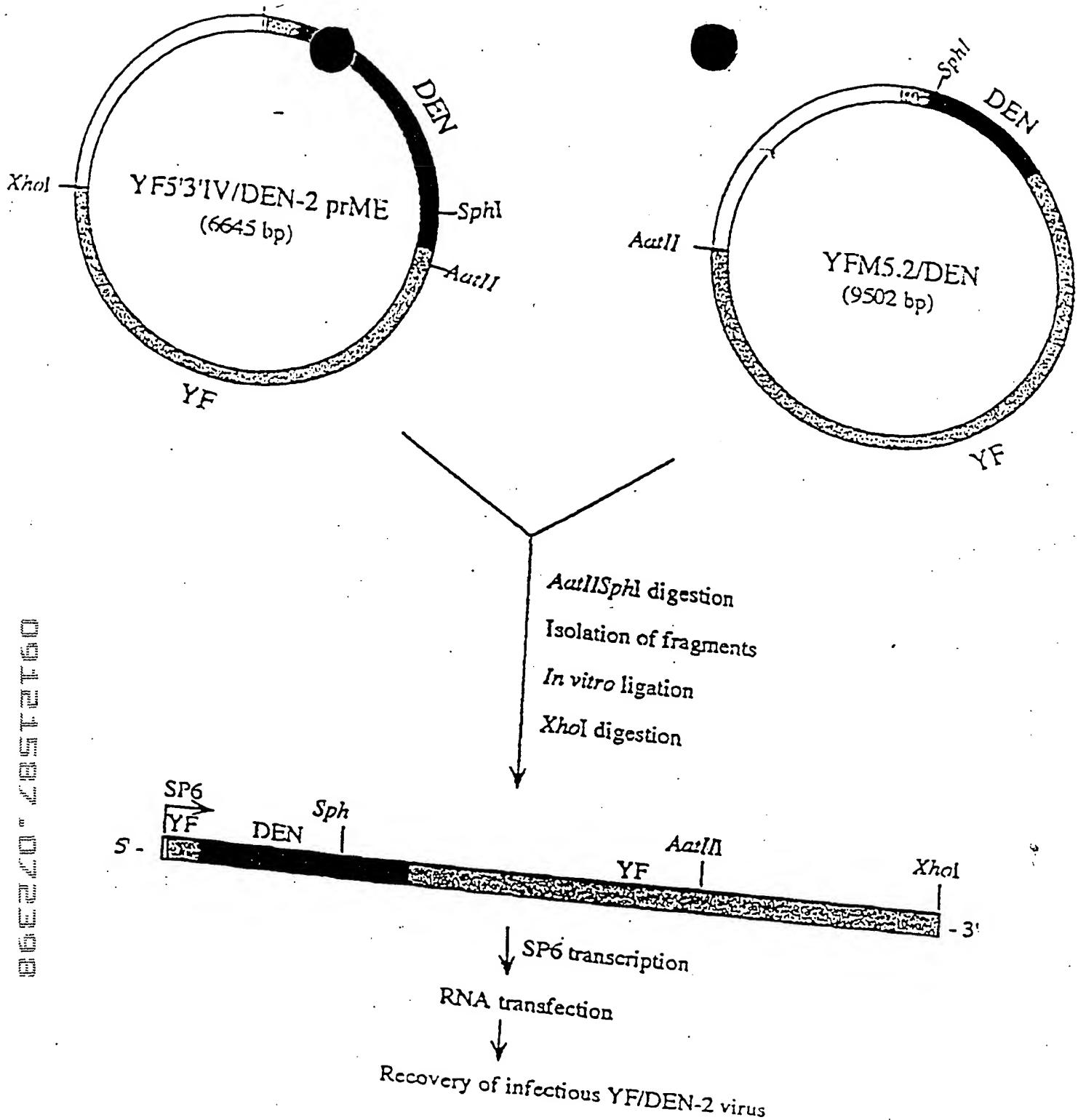


Fig. 15

Structure of modified YF clones expressing
E/NS1 Intergenic open reading frames

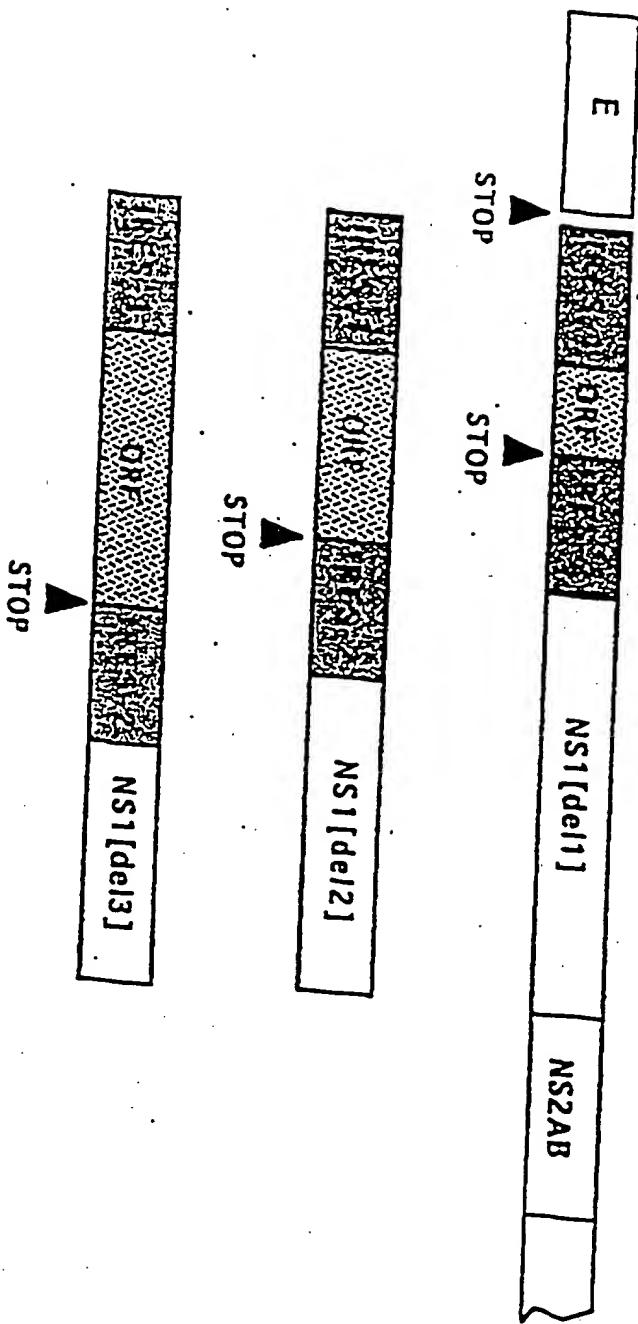


Fig. 16

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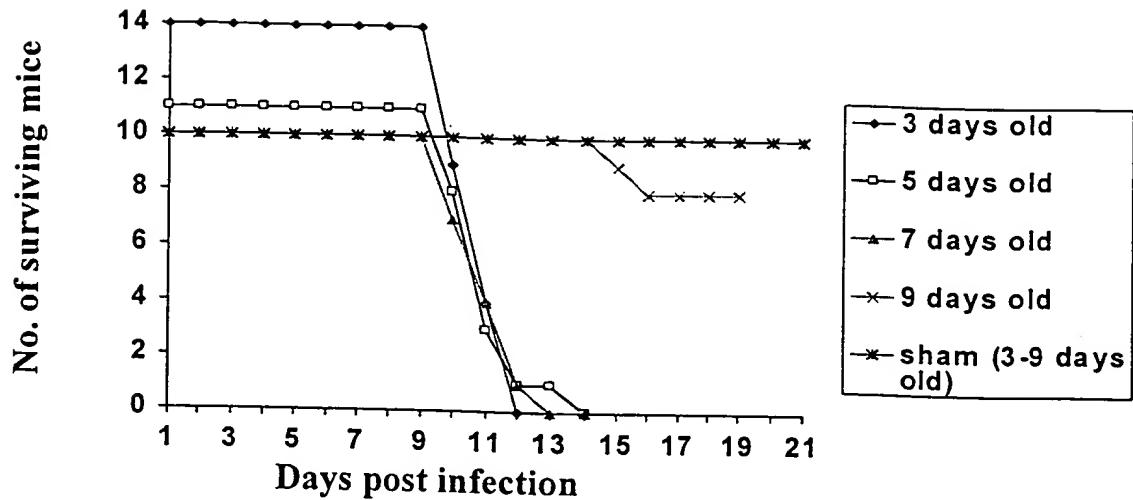


Figure 17. Neurovirulence phenotype of ChimeriVax™-Den2 in outbred (CD-1) suckling mice inoculated by the I.C. route with 10,000 PFU/0.02 ml.

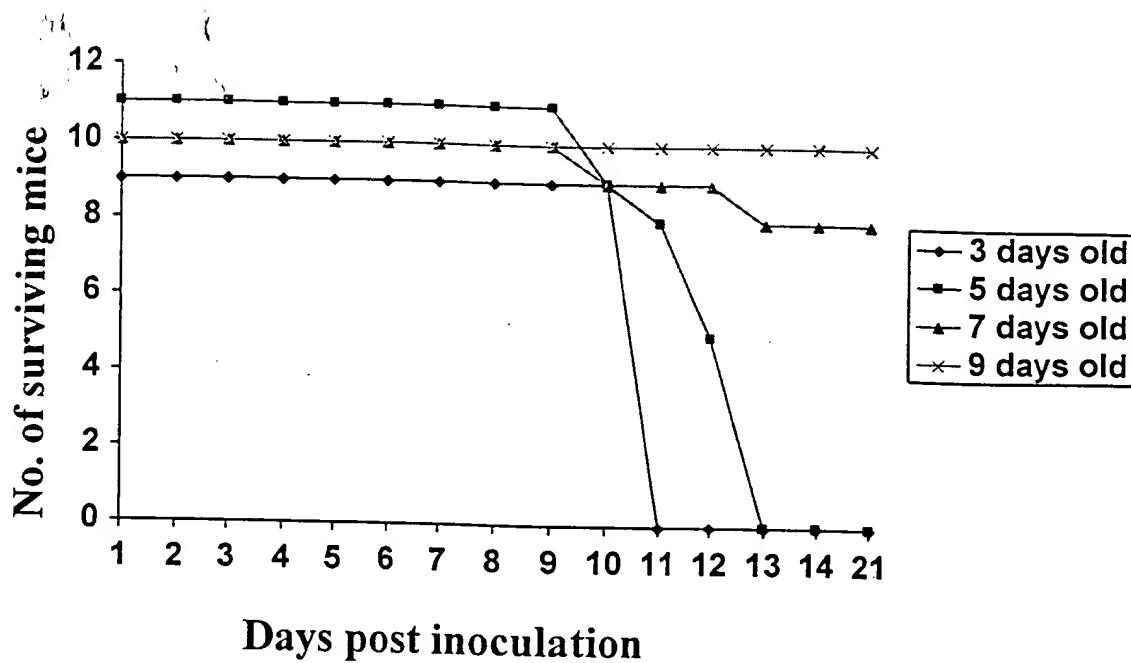


Figure 18. Neurovirulence phenotype of 17D vaccine (YF-Vax®) in outbred (CD-1) suckling mice inoculated by the I.P. route with 1000 PFU/0.02 ml.